Rubella Syndrome

Cardiovascular Manifestations and Surgical Therapy in Infants

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■ *Of nine patients under five months of age with cardiovascular manifestations of the rubella syndrome, six had patent ductus arteriosus. Three of these six also had pulmonary artery stenosis. One infant had bilateral isolated pulmonary artery stenosis. The significant clinical findings leading to the diagnosis of pulmonary artery stenosis were axillary murmurs in the presence of right ventricular hypertrophy. Demonstration of a gradient across the stenosis at the time of catheterization, together with cineangiography, established the diagnosis. In two cases ventricular septal defect was the only cardiac anomaly.*

Six babies under five months of age had interruption of a patent ductus arteriosus because of uncontrollable congestive heart failure or failure to thrive. Although growth failure was not necessarily due to heart disease, all were developing satisfactorily following operation.

Diagnosis and therapy of the cardiac complications of the rubella syndrome is possible in the first few months of life. Early recognition of cardiac defects in the young infant with the rubella syndrome permits aggressive medical management and in selected instances surgical therapy.

ATTENTION TO THE cardiovascular manifestations of the rubella syndrome has been given impetus by the nationwide rubella epidemic that occurred in 1964. Recent reports have indicated that, although patent ductus arteriosus is the most common associated cardiac anomaly, pulmonary artery stenosis and other congenital cardiovascular anomalies occur in this syndrome.[3,7] Recently we have seen nine infants with the rubella syndrome in whom cardiovascular anomalies were diagnosed by the age of five months. The purpose of this report is to describe the cardiac manifestations in these infants and to make note that early surgical treatment is indicated in selected instances.

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History

The pertinent clinical data are presented in Table 1. Six infants were found to have a patent ductus arteriosus. In three instances there was associated pulmonary artery stenosis. One infant was found to have isolated bilateral pulmonary artery stenosis and in two a diagnosis of ventricular septal defect was made on clinical grounds alone. Three of the infants were premature, weighing 1,644 gm or less at birth. The remaining six ranged from 2,438 gm to 3,714 gm in weight. Five patients had cataracts, bilaterally in three cases. Heart failure occurred in three patients. Five of the six patients who were operated upon had poor weight gain before operation.

A history of maternal exposure to rubella in early pregnancy was obtained in seven cases. The two other mothers were not aware of rubella exposure during pregnancy, but their infants had cataracts and proved patent ductus arteriosus, both characteristic of this syndrome. Confirmation by viral isolation was not obtained.

Physical Findings

A systolic thrill was palpable at the left sternal border in seven patients. A cardiac murmur was heard within the first two days of life in three infants, by one month in three infants, and by three and a half months in the remaining three. The most severely affected infant (Case 6, Table 1) had bilateral cataracts, petechiae, viral osteopathy of the long bones, patent ductus arteriosus and pulmonary artery stenosis. He was premature (1,474 gm). A continuous murmur was heard at birth.

Of the infants demonstrated to have patent ductus arteriosus, three had continuous murmurs. The remaining three had systolic murmurs that continued beyond the second sound in the pulmonary area but were not continuous. Two patients who clinically were thought to have small ventricular septal defects had systolic murmurs and thrills at the low left sternal border.

Axillary murmurs were clearly audible in the four patients with pulmonary artery stenosis. Three of these patients had an associated patent ductus arteriosus which was interrupted; however, the axillary murmurs were still heard. Bounding pulses were present in all of the six patients who had patent ductus arteriosus.

Electrocardiographic Findings

Severe right ventricular hypertrophy was noted in the patient with isolated pulmonary artery stenosis (Case 7, Table 1). Of the three patients with both patent ductus arteriosus and pulmonary artery stenosis, one had combined ventricular hypertrophy, one severe right ventricular hypertrophy, and one moderate right ventricular hypertrophy. Both patients with ventricular septal defect had borderline right ventricular hypertrophy. In one of the patients with isolated patent ductus arteriosus the electrocardiogram was considered normal, in another it was interpreted as showing left ventricular hypertrophy, and in the third it was consistent with combined ventricular hypertrophy.

TABLE 1.—*Clinical Data on Nine Patients with Rubella Syndrome*

Case No.	*Sex*	*Birth Date*	*Birth Weight Grams*	*History of Rubella*	*Age Murmur First Heard*	*Heart Failure*	*Cataracts*	*Thrill*	*Wide Pulse Pressure*	*Murmur*			*Diagnosis**
										Syst.	*Dias.*	*Cont.*	*Axil.*	
1	F	1/ 9/65	3,175	+	1 mo.	–	0	+	+	–	–	3/6	+	PDA (divided) PAS
2	F	1/24/65	2,438	–	3½ mo.	+	1	+	+	3/6	1/6	–	–	PDA (ligated)
3	F	10/ 1/65	3,714	+	2 mo.	+	0	0	+	3/6	1/6	–	–	PDA (divided)
4	F	2/11/65	2,863	–	2 mo.	–	1	+	+	–	–	3/6	–	PDA (divided)
5	M	7/20/65	1,503	+	1 mo.	+	0	+	+	3/6	1/6	–	+	PDA (ligated) PAS
6	M	11/23/65	1,474	+	Birth	–	2	+	+	–	–	3/6	+	PDA (divided) PAS
7	M	2/11/65	2,722	+	¾ mo.	–	2	0	–	2/6	–	–	+	PAS
8	F	11/23/65	2,835	+	1 day	–	0	+	–	3/6	–	–	–	VSD
9	F	2/23/65	1,644	+	2 days	–	2	+	–	3/6	–	–	–	VSD

*PDA—Patent ductus arteriosus; PAS—Pulmonary artery stenosis; VSD—Ventricular septal defect.

TABLE 2.—*Cardiac Catheterization Data on Seven Patients with Rubella Syndrome*

No. Case	Age at Time of Study (months)	Pressures, mm of Mercury				Oxygen Saturation					Ductus Entered
		RV	MPA	RPA	Ao	SVC	RA	RV	MPA	Ao	
1	4	40/0,5	40/25	19/12	100/50	68	71	64	81	93	Yes
2	4	55/0,5	55/30	–	75/35	–	62	62	81	94	Yes
3	4	30/0,5	30/15	–	100/50	60	61	63	80	–	Yes
4	3	60/0	55/25	–	70/25	71	69	70	82	94	Yes
5	3	60/0,5	60/25	–	100/55	–	70	78	83	90	Yes
6	7 (weeks)	50/0	50/12	20/5	85/40	78	78	80	80	94	Yes
7	2	55/0	45/10	15/5	–	70	74	–	73	95*	–

*Left atrial sample; RV—Right ventricle; MPA—Main pulmonary artery; RPA—Right pulmonary artery; Ao—Aorta; SVC—Superior vena cava; RA—Right atrium.

Roentgenographic Findings

Thoracic x-ray films of the patient with isolated pulmonary artery stenosis and of the two with small ventricular septal defects appeared to be normal. In the remaining six patients, pronounced cardiomegaly and increased pulmonary vasculature were demonstrated.

Cardiac Catheterization Findings

The data on seven patients in whom cardiac catheterization and cineangiographic studies were done are shown in Table 2. The ductus was entered from the pulmonary artery in five patients (Figure 1) and in a retrograde fashion from the aorta in another. Increased oxygen saturation in the pulmonary artery over that in the right ventricle was noted in all but one of the patients with patent ductus arteriosus (Case 6, Table 2). Right pulmonary artery stenosis was demonstrated by pull-out pressure recording in three patients, two of whom had associated patent ductus arteriosus. In addition to pressure recording data, pulmonary artery stenosis was demonstrated by cineangiography (Figure 2).

Surgical Intervention

The patent ductus arteriosus was interrupted in six patients before they were five months of age. In three of these infants the indication for operation was uncontrollable congestive heart failure; in the other three, the indications were cardiomegaly, pronounced increase in pulmonary vasculature, and failure to thrive. Only in Case 5 was the ductus found to be less than one-half the diameter of the aorta. In that patient, associated pulmonary artery stenosis was visualized and palpated in the hilum of the left lung. In one patient (Case 2) cardiac arrest occurred when the left lung was retracted to expose the patent ductus. Regular cardiac rhythm was restored immediately. No other operative complications were encountered.

All of the patients in the present series who were operated upon for patent ductus arteriosus have done well during follow-up periods of six to 16

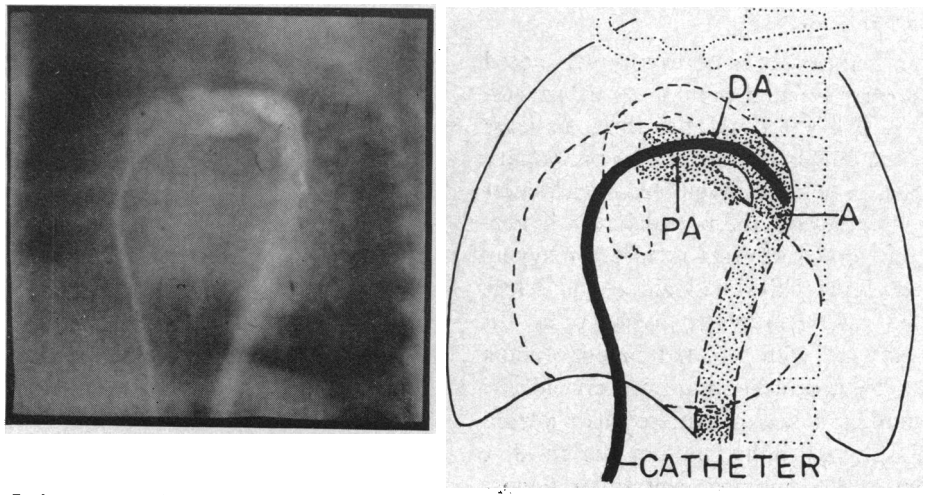

Figure 1.—Left anterior oblique projection. The course of the cardiac catheter is shown passing through the right heart into the pulmonary artery (PA), patent ductus arteriosus (DA), and into the descending thoracic aorta (A).

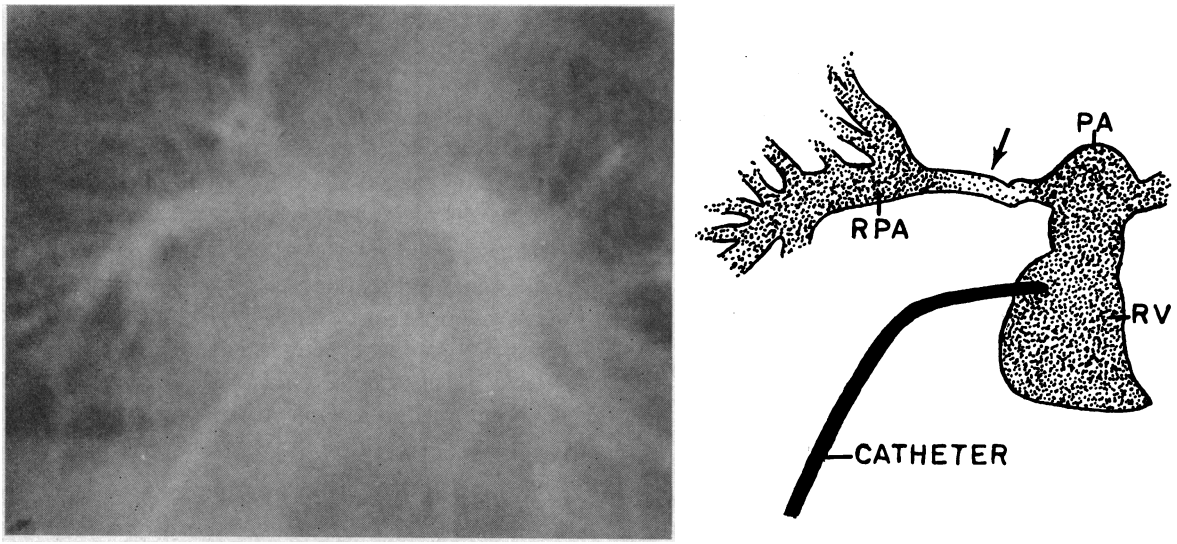

Figure 2.—The right ventricle (RV) and pulmonary artery (PA) are opacified in the AP projection. A narrowing in the right pulmonary artery (RPA) is demonstrated.

months. Heart size returned to normal within six weeks in all but one patient (Case 5) who has associated bilateral pulmonary artery stenosis.

Discussion

In 1941 Gregg[3] made the first observation that maternal rubella in early pregnancy was associated with congenital malformations of the heart. Stuckey[7] reported 27 patients, age three months to 12 years, with a variety of cardiac lesions associated with the rubella syndrome. He indicated that additional cardiac defects would be seen in one-fourth to one-third of the patients with patent ductus arteriosus. A report by Rowe[4] in 1963 helped focus attention on the association of pulmonary artery stenosis with the rubella syndrome. He emphasized the transmission of the murmur to the lateral chest wall as being the major physical finding permitting clinical diagnosis. A more recent communication by Rowe[5] indicates that pulmonary artery stenosis may occur as frequently as patent ductus arteriosus. Our case material confirms the findings of these observers.

In infants under six months of age, cardiac catheterization is recommended even in the presence of a continuous murmur in order to establish the diagnosis of patent ductus arteriosus. This will also serve to assess the presence and severity of other cardiac anomalies. Use of an end-hole catheter entails a possible pitfall in making the diagnosis of pulmonary artery stenosis in the presence of patent ductus arteriosus, since false high pres-

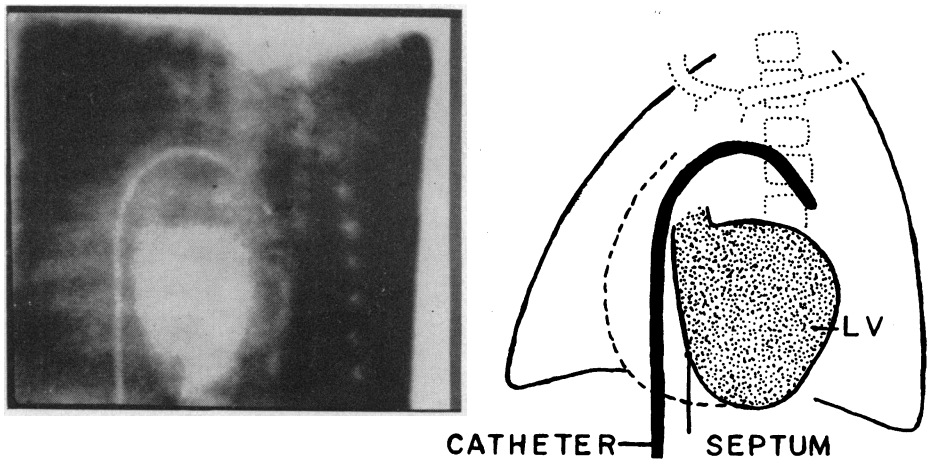

Figure 3.—Left anterior oblique projection, systolic phase. The radiopaque material has circulated through the lungs, left atrium, into the left ventricle (LV). The interventricular septum is demonstrated to be intact.

sure readings at the bifurcation of the pulmonary artery may be obtained when the tip of the catheter is within the ductus itself. An associated ventricular septal defect may also be ruled out by determination of oxygen saturation in each of the right heart chambers and with the use of cineangiography. Figure 3 shows an intact ventricular septum after circulation of radiopaque material into the left ventricle.

Three of the six patients in the present series who were successfuly operated upon for interruption of a patent ductus arteriosus have residual pulmonary artery stenosis with postoperative lateral chest wall murmurs as described by Emmanouilides.[2] These infants, however, have smaller hearts than they had before. They have normal electrocardiograms and they are gaining weight. Interrupting the ductus had duplicate beneficial effects in these patients. The increased pulmonary blood flow was reduced and thereby the flow across the stenotic area was decreased. This lowering of the pressure gradient in turn decreased right heart strain. We believe, therefore, that early interruption of the patent ductus was of particular benefit to these patients.

The patient with isolated bilateral pulmonary artery stenosis had been observed for 14 months at the time of this report. He has normal pulmonary blood flow, and although severe right ventricular hypertrophy continues, as demonstrated by electrocardiogram, he has no other signs of progressive disease. It should be noted, however, that even with such pronounced right ventricular hypertrophy, the right ventricular pressure at cardiac catheterization at two months of age was only 55 mm of mercury. If indicated, an angioplastic procedure with a venous onlay graft as described by Smith[6] can be done to relieve the pulmonary artery obstruction in patients of this kind.

The findings of Rowe and Emmanouilides that pulmonary artery stenosis usually occurs on the right side if it is unilateral was borne out in two of the cases in the present series (Cases 1 and 6). We feel this to be of clinical significance and that it should prompt the physician to auscultate in the right axilla as well as in the usual cardiac areas.

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